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UK Standards for Microbiology Investigations

Laboratory diagnosis of hepatitis C virus



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Amendment table

Each UK SMI document has an individual record of amendments. The amendments are listed on this page. The amendment history is available from standards@ukhsa.gov.uk.

Any alterations to this document should be controlled in accordance with the local document control process.

Amendment number/date	x/dd.mm.yy
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Section(s) involved	Amendment

*Reviews can be extended up to 5 years where appropriate

1 General information

[View general information](#) related to UK SMIs.

2 Scientific information

[View scientific information](#) related to UK SMIs.

3 Scope of document

This UK SMI provides a detailed review of initial and supplemental laboratory-based serological and Nucleic Acid Amplification Tests (NAAT) for the detection and exclusion of Hepatitis C virus (HCV). Refer to [UK SMI S 1: Acute infective hepatitis](#) for further information regarding clinical presentations of acute infective hepatitis and associated tests.

This document covers the different types of samples - whole blood, plasma and serum and the various methods of collection including venous and capillary blood sampling and dried blood spot (DBS) collection. It also addresses testing in specific patient groups. In addition, the algorithms aim to assist clinicians and laboratories in their decision making, by providing a framework for testing and the interpretation of results. Reporting criteria for commonly obtained test results are also provided.

CE marked assays should be validated and verified prior to use. If assays are to be used outside the scope for which the manufacturer has designated for its use, these should be validated and shown to be fit for purpose by the laboratory to suit its needs. For more information on CE marking, refer to the [IVD Directive](#) and for more information on validation of these CE marked assays, refer to UK SMI [Quality-related guidance](#)

This UK SMI is intended for use in the laboratory diagnosis of HCV infection within healthcare settings. It is not intended to cover:

- testing of blood prior to organ or blood donation (refer to the [SaBTO Guidance](#) on the microbiological safety of human organs, tissues and cells used in transplantation).
- testing methods or strategies commonly used in community testing such as POCT testing, self-sampling, or self-testing.
- testing of specimens other than blood, plasma and serum obtained by venepuncture, such as oral fluid and saliva.
- ongoing monitoring tests used for those with a confirmed diagnosis of HCV.

For the investigation and management of occupational exposure, refer to UKHSA (formerly PHE) and HSE guidelines (2-5).

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For blood-borne virus (BBV) testing following dialysis away from base (DAFB), refer to DHSC guidelines (6).

For the management and treatment of Hepatitis C, refer to the EASL recommendations on treatment of hepatitis C and BHIVA guidelines for the management of hepatitis viruses in adults infected with HIV (7,8).

This UK SMI should be used in conjunction with other UK SMIs.

Abbreviations

Abbreviation	Definition
HCV	hepatitis C virus
BBV	Blood-borne viruses
DBS	Dried blood spot
POCT	Point of care testing
PWID	People who inject drugs
NAAT	Nucleic acid amplification test
DAA	Direct-acting antivirals

Definitions

For all antibody and NAAT testing, the following definitions apply:

Reporting stage for serology

These terms are used for final or preliminary reports.

Reactive – Report-stage confirmed reactive result.

Not reactive – Report-stage not reactive result.

Equivocal – Reactive result that cannot be confirmed.

Reporting stage for molecular assays

These terms are used for final or preliminary reports.

Scenarios	Qualitative result	Quantitative actual value	Quantitative Log10 of actual value
1	Detected	Actual value	Calculated log from actual value of the assay
2	Detected	Below the lower limit of detection of the assay	Calculated to the lower limit of the assay value
3	Detected	Above the upper limit of detection of the assay	Calculated to the upper limit of the assay value
4	Not detected	Below the lower limit of detection of the assay	Calculated to the lower limit of the assay value
5	Inhibitory	Not applicable	Not applicable
6	Insufficient	Not applicable	Not applicable
7	Invalid	Not applicable	Not applicable

4 Introduction

In the UK, hepatitis C virus infection remains a significant public health concern. The UK government has aligned its national efforts with the WHO's goal of eliminating HCV (and HBV) globally as a public health threat by 2030. In 2016 the UK government committed to the WHO's Global Health Sector Strategy on Viral Hepatitis (GHSS) and in May 2022 adopted the updated 2022-2030 strategy.

Significant progress has been made towards the elimination of HCV across the UK (9-12). Improvements in testing, including the use of point-of-care testing (POCT) in hard-to-reach areas, and opt-out testing programmes in emergency departments along with accessible treatments such as direct-acting antivirals (DAAs) are key drivers in hepatitis C elimination efforts (13-17). These advancements, if continued at the current rate, are predicted to achieve an 80% reduction in chronic HCV by 2030 compared to 2015 as the baseline (18,19).

4.1 Hepatitis C Virus (HCV)

Hepatitis C virus (HCV) is a blood-borne virus of the *Flaviviridae* family and a member of the Hepacivirus genus (20-22). It is a single stranded, positive sense enveloped RNA virus with a genome of approximately 9600 bases (20). There are eight genotypes of HCV (1 to 8) to date, each with multiple subtypes that are distributed worldwide (23-26). The most common genotypes in the UK are HCV genotypes 1 and 3 (27,28).

4.2 Stages of HCV infection

New acute HCV infections are usually asymptomatic (85 - 90% cases) and therefore acute infection is rarely diagnosed. Around 30% (15 - 45%) of infected persons spontaneously clear the virus within 6 months of infection without any treatment (21,29-31). Spontaneous viral clearance is rare beyond 4 to 6 months of infection, therefore HCV RNA detectable for longer than 6 months is defined as Chronic HCV infection (21,29-31). Levels of HCV RNA remain relatively stable over time in chronically infected patients.

HCV reinfection is defined as the reappearance of HCV RNA at least 6 months after a sustained viral clearance (SVR) with a different HCV genotype or strain (7).

4.3 HCV diagnostic approaches

Routine laboratory diagnosis of established infection is commonly based upon the detection of antibodies for the virus using serological methods, followed by the detection of the virus using HCV RNA NAAT on the same sample to confirm viraemia (20,32-37).

The approach to HCV infection diagnosis and monitoring is tailored to individual patient circumstances, considering factors such as immune status, pregnancy, and risk behaviours. In the UK, since the introduction of screening of blood and blood-derived products, HCV is most common in people who inject drugs (PWID), with 10% and 70% antibody prevalence for those injecting for 2 years and 15 years respectively (18,19,38). This is especially the case within PWID populations in prison or those experiencing homelessness.

Antibodies to HCV are detected using first line Enzyme Linked Immunosorbent Assays (ELISA), Enzyme Immunoassays (EIA), Chemiluminescent Immunoassays (CLIA) or in the past with second line immunoblots (39). Assays have been developed to detect antibodies to an increasing range of viral proteins, from second generation (core proteins and non-structural proteins 3 and 4), third generation (also with non-structural protein 5) and now fourth generation (also with HCV capsid antigen) (35,40).

The diagnosis of recently acquired or chronic HCV infection is based on the detection of HCV RNA by a qualitative or both qualitative and quantitative molecular methods (7). An HCV RNA assay with target sensitivity level of 15 IU/mL or lower is recommended (7). Reflex NAAT testing is recommended to streamline the HCV care pathway (41-43). Molecular methods are recommended over HCV core antigen testing for confirmation due to the higher rates of false negatives and lower sensitivity compared to HCV RNA NAAT (44-46). Therefore, hepatitis C core antigen testing will not be discussed further within this document.

4.4 Types of HCV diagnostic tests and markers of infection

- **HCV RNA** is a marker of replicating virus in peripheral blood. HCV RNA may be detected as early as 1 to 3 weeks after initial infection, approximately 1 month before the appearance of total HCV antibodies.
- **Immunoglobulin G (IgG) antibodies** emerge after IgM antibodies and persist throughout the course of HCV infection. Most assays are designed to detect IgG which become detectable at approximately 8 to 12 weeks following exposure (47).

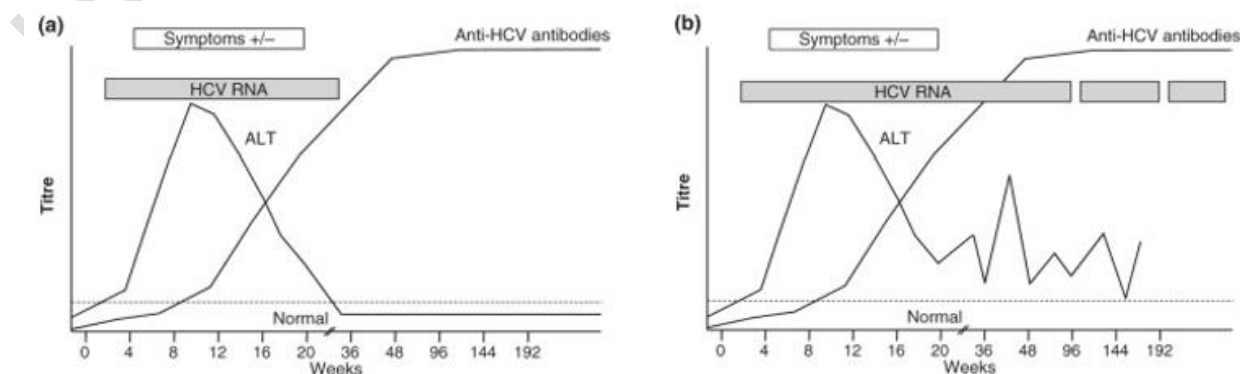


Figure 1. Kinetics of virological markers during acute (a) and chronic (b) hepatitis C virus (HCV) infection (1).

5 Technical information and limitations

5.1 Sample types and collection methods:

Dried Blood Spots (DBS) and capillary blood samples have been adapted for use in HCV serology and qualitative NAAT for HCV diagnosis. (48-51). These samples are useful in identifying individuals with chronic HCV but may have a lower sensitivity for monitoring therapeutic response (48,52). Therefore, appropriate local validation and/or verification is required prior to their use to ensure accuracy and effectiveness in both diagnostic and monitoring context.

5.2 Immunoassays:

HCV antibody tests:

The limitations of antibody tests primarily arise when they are used alone, particularly in low-risk groups or in immunocompromised individuals. In populations with low exposure risk, a low-level positive result may be reflective of a false positive (53). In addition, antibodies can take a long time to develop, typically around 5 to 12 weeks in the immunocompetent and several months in immunocompromised leading to delayed detection. This may limit the clinical utility of antibody tests during the window period, and in immunocompromised patients due to delayed or absent seroconversion (53,54). In addition, antibody tests cannot distinguish between historical HCV infection with sustained viral clearance and reinfection with a different HCV genotype.

Individuals who are immunocompromised or with risk factors should undergo HCV RNA detection with PCR (53-55).

5.3 Molecular methods

HCV RNA is a marker of active viral replication, but low-level results should be interpreted with caution as they may have various causes including intermittent viraemia, assay variability and antiviral treatment response. Laboratories should provide detailed quantification for more informed clinical interpretation. When low-level positivity is observed, careful evaluation is required with further testing or clinical correlation as appropriate.

In addition, when samples with low viral load are diluted to bring them within the assay's quantifiable range, there is a risk that viral concentration could either fall below the detection threshold or be at the lower limit of detection. For example, a negative HCV RNA after a 2-fold dilution may suggest that the original viral load was too low to be detected after dilution, making current infection extremely unlikely. Reporting the dilution factor helps clinicians make a more informed decision, particularly in low-level positive results or low viral loads.

NAAT Inhibition:

It has been recognised that samples may contain substances that can inhibit amplification, potentially causing false negative results (33). It is recommended to use an inhibition control in NAAT testing (1). Internal and cellular controls exist within most commercial kits. Many NAATs are able to remove inhibitory substances during the nucleic acid extraction process. In duplex or multiplex assays, where several targets may be detected, competitive inhibition may be observed. The test manufacturers' instructions should be followed as they may contain a list of substances which have been identified as inhibitory through verification and validation. The laboratory may consider regular monitoring of inhibition levels and positive rates.

Contamination:

The risk of contamination should always be considered when using NAAT.

See also [UK SMI Q 4 Good laboratory practice when performing molecular amplification assays](#).

6 Safety considerations

The section covers specific safety considerations related to this UK SMI and should be read in conjunction with the general [safety considerations](#) (56-74).

6.1 Specimen collection, transport, and storage

Use aseptic technique to collect blood.

Collect adequate and appropriate specimens in appropriate CE marked leak proof containers and transport in sealed plastic bags.

Compliance with postal, transport and storage regulations is essential.

This guidance should be supplemented with local COSHH and risk assessments.

Refer to current guidance on the safe handling of all organisms documented in this UK SMI.

6.2 Specimen handling and processing

Laboratory procedures that give rise to infectious aerosols must be conducted in a microbiological safety cabinet.

Refer to current guidance on the safe handling of all organisms documented in this UK SMI.

The above guidance should be supplemented with local COSHH and risk assessments.

7 Methodology

7.1 Pre-testing considerations

WHO recommends that all adults have access to and be offered HCV testing with linkage to prevention, care and treatment services with more focused testing for individuals at increased risk of infection (21). Additionally, in settings where the general population has an HCV antibody seroprevalence of $\geq 2\%$ or $\geq 5\%$ (21). WHO also recommends blood donor screening, as well as focused or targeted testing of specific high-risk groups, including migrants from endemic regions, health-care workers, people who inject drugs (PWID), people in prisons and other closed settings, men who have sex with men (MSM), sex workers and HIV-infected persons (21).

Targeted and more frequent hepatitis C screening in people who are at increased risk of infection is also strongly recommended by UK bodies such as UKHSA, British HIV Association, British Association of Sexual Health and HIV, and National Institute for Health and Care Excellence to address the need to improve rates of earlier diagnosis (8,18,21,36).

Specific groups are usually routinely screened for HCV by specialist service providers. These include blood, organ or tissue donors, end-stage kidney disease patients and healthcare workers following occupational exposure.

It should be noted that routine testing of pregnant women for HCV infection is currently not recommended. However, pregnant women at increased risk of infection should be tested.

7.1.1 Specimen type:

Whole blood, serum or plasma DBS or finger capillary

Note: Venous blood is the preferred specimen for hepatitis C virus testing. However, alternative sample types can also be used. DBS or finger capillary samples can be used in HCV serology and qualitative NAAT for HCV diagnosis.

Use of specific sample types in individual assays is subject to local verification and validation requirements, alongside the manufacturer's instructions.

7.1.2 Specimen collection and processing:

For safety considerations refer to Section 6.

Venous blood is the preferred specimen for HCV testing. DBS and capillary blood samples are increasingly employed in hard-to-access populations such as in prisons and in people who inject drugs (PWID).

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Use of specific sample types in individual assays is subject to local verification and validation requirements, alongside the manufacturer's instructions.

Specimens collected in EDTA, or serum separator tubes are generally acceptable for testing. Please refer to manufacturer instructions for specimen acceptability.

Providing adequate sample volume is essential for maintaining test sensitivity and accuracy. If a sub-optimal volume is provided (perhaps due to dilution) this must be reported, and a repeat sample requested.

Refer to local laboratory protocols or the manufacturer's instructions for specific requirements on serum or plasma separation for NAAT.

7.1.3 Specimen transport, storage, and retention

For safety considerations refer to Section 6.

Specimens should be transported and processed as soon as possible (75). If processing is delayed, refrigeration is preferable to storage at ambient temperature (75).

Note: Specimens for NAAT can be stored long-term at - 20° or - 70°C to minimise RNA loss (76).

Samples should be retained in accordance with The Royal College of Pathologists guidelines 'The retention and storage of pathological records and specimens' (73).

7.1.4 Test selection:

The choice of test can be influenced by risk factors.

Please note that HCV RNA NAAT is recommended as the initial test in certain patient populations or situations to avoid missing cases of HCV infections. This ensures early detection and appropriate management.

Immunocompetent people:

The initial screening assay should be a 3rd or 4th generation antibody assay which if positive should be followed by a confirmatory HCV RNA NAAT. People at risk of acute HCV infection or HCV reinfection – screen using HCV RNA NAAT. There is no need for second antibody assay because it is of very little clinical utility.

Immunocompromised people:

Screen using HCV RNA NAAT.

For immunosuppression definitions, refer to UKHSA [guidelines on post exposure prophylaxis for varicella or shingles](#).

Pregnant women and infected babies:

Pregnant women who are at increased risk for hepatitis C virus infection should be tested at their prenatal visits by testing for HCV antibodies. If the initial results in pregnant women with on-going risk factors for hepatitis C virus infection are negative, this should be repeated later in the third trimester (77,78). It should be noted that routine testing of pregnant women for HCV infection is currently not recommended (79).

Mothers with evidence of hepatitis C virus antibodies who are stably HCV RNA negative are highly unlikely to transmit HCV to the baby (80-82). Babies born from HCV RNA NAAT negative, HCV antibody positive mothers do not require routine testing (83).

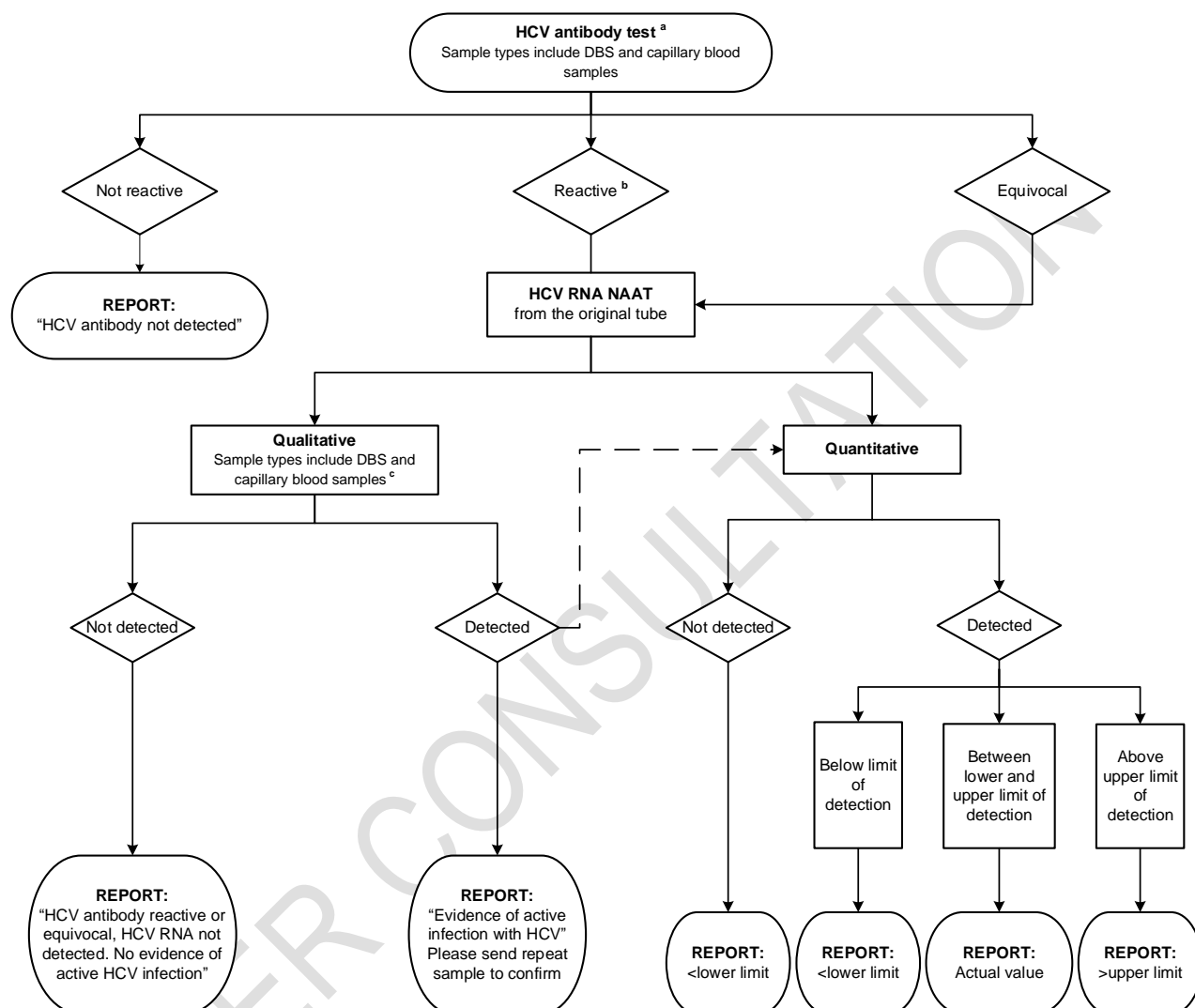
For women who have acquired infection during pregnancy, but have cleared viraemia, the baby should be followed up as described in algorithm 7.3. It should also be noted that consideration should be given to investigate previous pregnancies or partner of current HCV positive mothers.

For babies born to a woman who has injected drugs, if the mother is unavailable to consent for testing and there is evidence of suspected HCV infection, test the baby for HCV antibody and follow algorithm 7.3 if the baby is HCV antibody positive. If the baby is HCV antibody negative, then this is highly predictive of absence of infection providing the exposure risk is more than 6 months ago (81).

A negative HCV RNA NAAT result in babies may reflect resolution of infection (>25% resolved), fluctuating RNA level or a lab error. Therefore, an antibody test should be performed between 12 - 18 months (84,85). Please note that other guidelines do not always advocate early NAAT testing in children (83).

Infants infected with HCV should be monitored and assessed clinically every 6 - 12 months to identify any risks of progressive liver fibrosis during childhood (83,86).

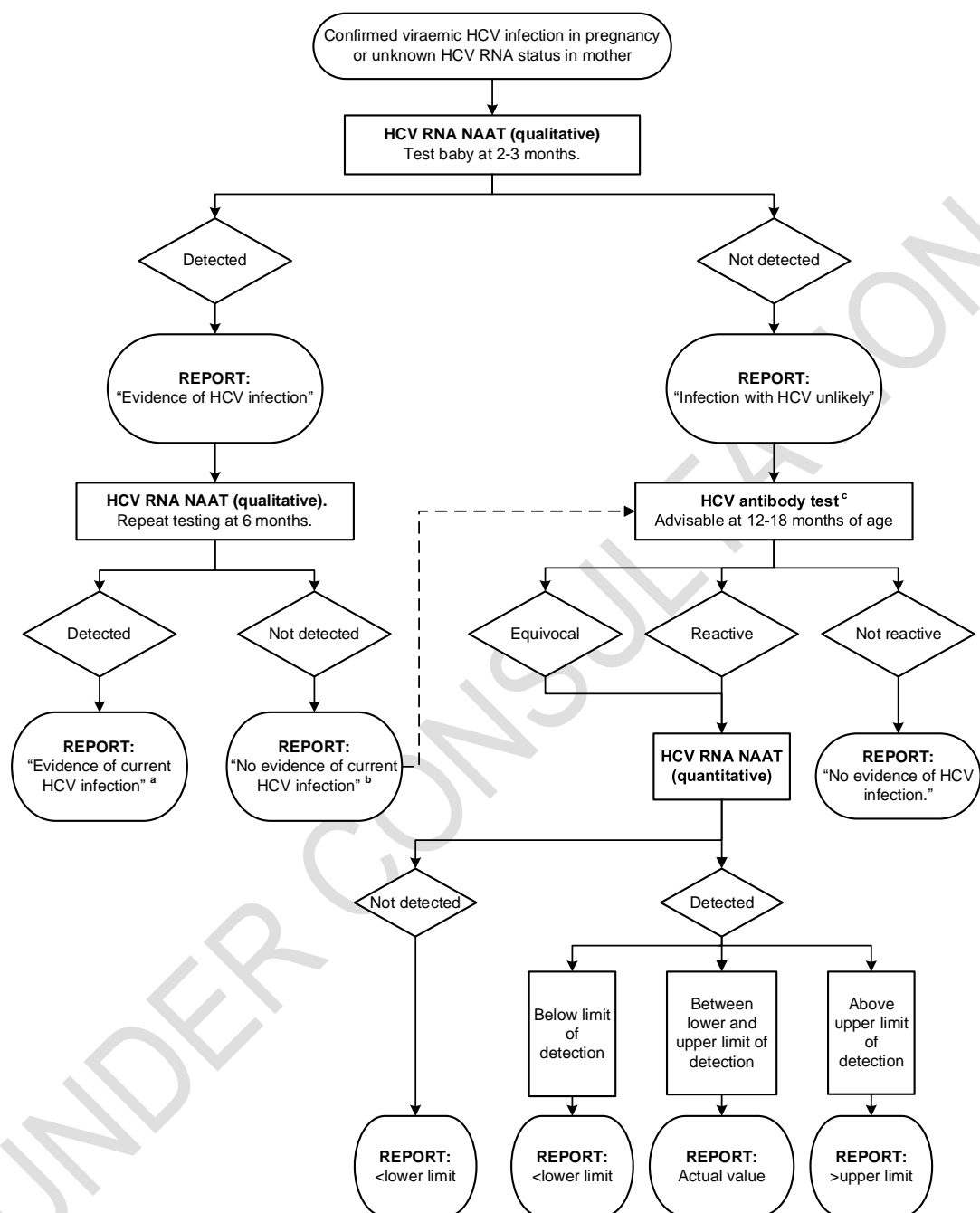
7.2 Investigation of hepatitis C infection by HCV antibody testing confirmed by HCV RNA NAAT (7,33,37,87)



Footnotes:

- Screening directly with HCV RNA NAAT is required for certain patient groups, particularly those who are immunocompromised or when the risk of recent or ongoing infection is high, as NAAT is more reliable in these cases than HCV antibody testing.
- Report at this stage as an interim report if additional testing will be delayed and the result may have immediate significance for patient management; suggested wording "Initial HCV antibody reactive. Hepatitis C RNA result to follow".
- Follow up with quantitative HCV RNA NAAT is recommended for both DBS and capillary blood samples to assess viral load and guide treatment decision.

7.3 Mother-to-child transmission of hepatitis C infection (88-90)



Footnotes:

- a) Advise referral to Paediatric Hepatologist or Paediatric Infectious Disease Specialist for further assessment/ treatment.
- b) Request repeat sample. Laboratories may wish to repeat discordant results.

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- c) If antigen/antibody assays are to be used, they should be carefully assessed, and antigen negative results followed by a NAAT test. **Note:** If HCV antigen only assays are used, ensure that NAAT test is performed.

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7.4 Interpreting and reporting laboratory results

The final result should be able to distinguish active HCV infection from resolved infection using a combination of antibody and NAAT tests.

It is recommended that HCV test reports include the dilution factor to aid in the interpretation of low-positive results and support clinical decision-making.

Following an initial (first sample) positive result, it is best practice to request a repeat sample.

Table 1. Investigation of hepatitis C virus infection by HCV antibody testing confirmed by NAAT.

	1 st Assay	2 nd Assay	Interpretative comments	Notes
	HCV Ab	HCV NAAT		
1	Not reactive	Not tested	HCV antibody not detected.	In the case of suspected acute hepatitis C or in immunocompromised patients, HCV RNA testing should be part of the initial evaluation.
2	Not reactive	RNA Detected [quantitative value as appropriate]	<p>Evidence of active HCV infection.</p> <p>Advise referral to an appropriate specialist for further assessment/treatment.</p> <p>Hepatitis A and B vaccine recommended if appropriate.</p>	<p>Indicates either acute HCV infection or possibly a chronic infection in an immunocompromised patient.</p> <p>Please ensure hepatitis A and B vaccination status is known and vaccination given if needed.</p> <p>Consider requesting HCV genotyping and other BBV testing unless already performed.</p>

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	1 st Assay	2 nd Assay	Interpretative comments	Notes
	HCV Ab	HCV NAAT		
3	Reactive or Equivocal	RNA detected [quantitative value as appropriate]	<p>Evidence of active HCV infection.</p> <p>Advise referral to an appropriate specialist for further assessment/treatment.</p> <p>Hepatitis A and B vaccine recommended if appropriate.</p>	<p>HCV antibody detected in the presence of HCV RNA allows one to infer with confidence that the HCV antibody reaction is a true positive.</p> <p>Please ensure hepatitis A and B status is known and vaccination given if needed.</p> <p>Consider requesting HCV genotyping and other BBV testing unless already performed.</p> <p>If initial antibody assay is equivocal and RNA detected, this may be recent infection. Consider review of clinical and results history, that is, can seroconversion to HCV antibodies be documented.</p>
4	Reactive or Equivocal	RNA not detected	No evidence of active HCV infection.	<p>HCV antibody positive result may indicate past HCV infection.</p> <p>EASL 2020 recommend that “Anti-HCV antibody-positive, HCV RNA-negative or HCV core antigen-negative patients with suspected <i>de novo</i> recently acquired HCV infection should be retested for HCV RNA 12 and 24 weeks later to confirm definitive clearance” (7).</p>

Table 2. Investigation of hepatitis C virus infection in babies of women confirmed to have HCV infection during pregnancy using both NAAT and HCV antibody test.

	HCV NAAT at 2-3 mths	HCV NAAT at 6 mths	Interpretative comments	Notes
1	RNA detected [quantitative value as appropriate]	RNA detected [quantitative value as appropriate]	<p>At 2-3 months,</p> <p>Evidence of HCV infection.</p> <p>Please send EDTA plasma for a repeat HCV NAAT at 6 months.</p> <p>Advise referral to Paediatric Hepatologist or Paediatric Infectious Disease Specialist for further assessment/treatment.</p> <p>At 6 months,</p> <p>Evidence of current HCV infection.</p> <p>Advise referral to Paediatric Hepatologist or Paediatric Infectious Disease Specialist for further assessment/treatment.</p> <p>Hepatitis A virus and B virus vaccine recommended if appropriate.</p>	<p>In the case of suspected acute hepatitis C virus or in immunocompromised patients, HCV RNA testing should be part of the initial evaluation.</p> <p>Please ensure hepatitis B virus vaccination status is known and vaccination given if needed.</p> <p>Consider requesting HCV genotyping and other BBV testing unless already performed (79).</p>

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2	RNA detected [quantitative value as appropriate]	RNA not detected [quantitative value as appropriate]	<p>At 2-3 months,</p> <p>Evidence of HCV infection.</p> <p>Please send EDTA plasma for a repeat HCV NAAT at 6 months.</p> <p>Advise referral to Paediatric Hepatologist or Paediatric Infectious Disease Specialist for further assessment/treatment.</p> <p>At 6 months,</p> <p>No evidence of current HCV infection.</p> <p>Request repeat sample for retesting.</p> <p>Advise HCV antibody testing at 12-18 months to confirm clearance of maternal antibody.</p>	
3	RNA not detected	Not tested	<p>At 2- 3 months,</p> <p>Infection with HCV unlikely.</p> <p>Advise HCV antibody testing at 12-18 months.</p>	

Following a negative HCV RNA result at 2-3mths of age, testing for HCV antibodies using HCV antibody test at 12-18 months			
	HCV antibody Test at 12-18mths	Interpretative comments	Notes
4	Detected	<p>No evidence of active HCV infection.</p> <p>Please send EDTA plasma for a repeat HCV NAAT to confirm evidence of infection.</p>	<p>HCV antibody positive result may indicate past HCV infection.</p> <p>EASL 2020 recommend that “Anti-HCV antibody-positive, HCV RNA-negative or HCV core antigen-negative patients with suspected <i>de novo</i> recently acquired HCV infection should be retested for HCV RNA 12 and 24 weeks later to confirm definitive clearance” (7).</p> <p>Suggest a repeat sample to confirm HCV antibody status. Please note that undetectable HCV RNA does not exclude current infection because viraemia may be intermittent. Suggest testing a follow-up blood for HCV NAAT to investigate possible fluctuating viraemia (7).</p>
5	Not detected	No evidence of HCV infection.	

Confirmation of HCV antibody test performed at 12-18 months using HCV RNA NAAT			
	HCV NAAT at 12-18 mths	Interpretative comments	Notes
6	RNA detected [quantitative value as appropriate]	<p>Evidence of HCV infection.</p> <p>Please send EDTA plasma for a repeat HCV NAAT to confirm evidence of infection.</p> <p>Advise referral to Paediatric Hepatologist or Paediatric Infectious Disease Specialist for further assessment/treatment.</p>	
7	RNA not detected	<p>No evidence of HCV infection.</p> <p>Likely to be resolved infection or maternal antibody if less than 18 months.</p> <p>Please repeat HCV antibody test after 18 months.</p>	

8 Public health management

All confirmed cases of HCV infections should be reported to local public health authorities.

For information regarding notification refer to:

<https://www.gov.uk/government/collections/notifications-of-infectious-diseases-noids>

For further information on public health management refer to:

<https://www.gov.uk/government/collections/hepatitis-c-guidance-data-and-analysis>

In addition to reporting new positive diagnosis to UKHSA Health Protection Teams, participating laboratories should also report into sentinel surveillance programmes for HCV.

In the UK, guidance for hepatitis C infected health care workers (HCW) is available.

See link: <https://www.gov.uk/guidance/bloodborne-viruses-in-healthcare-workers-report-exposures-and-reduce-risks>

For the final report published on the Infected Blood Inquiry in May 2024 refer to the following link: [Reports | Infected Blood Inquiry](#)

9 Public health responsibilities of diagnostic laboratories

Diagnostic laboratories have public health responsibility as part of their duties. Amongst these are additional local testing, or referral to further characterise the organism as required, primarily for public health purposes e.g. routine cryptosporidium detection; serotyping or microbial subtyping; and a duty to refer appropriate specimens and isolates of public health importance to a reference laboratory.

Diagnostic laboratory outputs inform public health intervention, and surveillance data is required to develop policy and guidance forming an essential component of healthcare. It is recognised that additional testing and referral of samples may entail some costs that has to be borne by the laboratory but in certain jurisdictions these costs are covered centrally.

Diagnostic laboratories should be mindful of the impact of laboratory investigations on public health and consider requests from the reference laboratories for specimen referral or enhanced information.

References

An explanation of the reference assessment used is available in the [scientific information section on the UK SMI website](#).

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